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HRT use in 2001 and 2004 in The Netherlands—A world of difference

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Abstract

Objective: Did the publication of the Women Health Initiative (WHI) trial in 2002 and the Million Women Study (MWS) in 2003 lead to changes in prescription rates of hormone replacement therapy (HRT). Therefore, we compare the prescribing of HRT in 2004 (after) with that of 2001 (before the publications) in The Netherlands.
Method: Community pharmacy dispensing data from a population of approximately 500,000 patients in The Netherlands. Women aged 40–74 years to whom at least one HRT prescription was dispensed in 2001 or 2004 were included. Annual prevalences of HRT in 2001 and 2004 and the percentage change (2004 versus 2001) were calculated for overall HRT (excluding vaginal products) and per HRT category (combined estrogens and progestagens, estrogens only, tibolon and vaginal preparations) and age category.
Results: In 2001, 5.64% of the women aged 40–74 used HRT and this percentage declined to 2.39 in 2004. The use of vaginal products among these women did not change, 1.76% in 2001 and 1.65% in 2004. The percentage change was highest in the opposed HRT group (66% decrease) and in women aged 50–54 (64.4% decrease). In 2004, compared with 2001, the proportion of long-term users (>3 year) increased with 12.7%.
Conclusions: In The Netherlands, after publication of the WHI study and the MWS the prescribing of HRT fell dramatically whereas the prescribing of vaginal products did not change. Future patterns of HRT use should be monitored to know whether this decrease will be sustained.

Keywords: Hormone replacement therapy (HRT); Change in prescribing; Low potency estrogens/vaginal products; Opposed HRT; Unopposed HRT; Tibolon

1. Introduction

In The Netherlands, hormone replacement therapy (HRT) is licensed for the alleviation of climacterial symptoms and the prevention of osteoporosis, however in daily practice, it was mainly prescribed for treatment

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of vasomotor symptoms. HRT preparations used for this purpose are either combined estrogens and progestagens (opposed) or estrogens alone (unopposed) or tibolon. Vaginal applications, containing estriol or dienestrel, are licensed for the relief of urogenital symptoms.

Before 2002, HRT had been regarded as an intervention with great potential benefits in terms of cardiovascular disease prevention and osteoporosis treatment [1–3]. The publications of the Women Health Initiative (WHI) trial results [4–6] and the results of the observational Million Women Study (MWS) [7] reported increased rates of breast cancer, coronary heart diseases, stroke, dementia and venous thromboembolism and decreased rates of hip fractures and colorectal cancer in postmenopausal women using long-term HRT. Both studies led to much attention and debate in the medical and the lay press.

As a consequence, shortly after the publication of the MWS the Dutch associations of gynaecologists and general practitioners clearly stated that HRT should be prescribed only in women with severe vasomotoric complaints in the lowest effective dose and for a short period. According to the general practitioners this period should not exceed 6 months and the recommendations of the gyneacologists stated that the treatment should be evaluated every 6–12 months [8,9]. The European Medicines Agency for Drug Safety (EMEA) stated in a position paper that for the initiation and continuation of HRT, the minimum effective dose for the shortest duration should be used. And in all cases, a careful appraisal of the risks and benefits should be undertaken at least annually and HRT should only be continued as long as benefits overweighs risks [10].

The aim of this report is to compare the use of HRT in The Netherlands in 2004, after publication of the WHI trial and the MWS results, with the use in 2001, the year before these publications. In addition, we compared the duration of use among HRT-users before and after publication of both studies.

2. Methods

This study was performed with the InterAction Database (IADB), which contains prescription drug dispensing data from community pharmacies in the northern and eastern part of The Netherlands. The IADB covers all prescriptions from an estimated population of approximately 500,000 since 1999 [11,12]. Each prescription record contains among others name of the drug, ATC-code, date of dispensing and amount dispensed. Each patient has a unique, though anonymous identifier. Date of birth and gender of patients are available. Due to a high patient–pharmacy commitment in The Netherlands and sophisticated pharmacy software, the medication records for each patient are virtually complete [13]. This database comprises all prescriptions, regardless of insurance or reimbursement status, apart from drugs dispensed during hospitalisations. Note that almost all HRT preparations are fully reimbursed. Only for transdermal oestrogen/progestagen preparations a patient's copayment is required.

2.1. Study population and design

All women aged 40–74 years, to whom at least one HRT prescription was dispensed in 2001 or in 2004 were selected from the IADB. Women who received HRT prescription were classified into four categories: (I) those who received conjugated estrogens or estradiol and progestagens either in a fixed combination or separately (opposed), (II) those who only received estrogens (conjugated estrogens or estradiol) (unopposed), (III) women who got tibolon and (IV) women who received low potency estrogens (estriol or dienestrel) mainly a vaginal application for vulvar vaginal atrophy. Tibolon is a synthetic steroid with weak estrogenic, progestogenic and androgenic properties [14]. Prevalence of HRT prescribing was estimated per year (2001 and 2004) and was defined as the number of women (aged 40–74) to whom any HRT prescription was dispensed per 100 women in the population covered by the IADB. Annual prevalence was stratified per HRT category and 5-years age categories. The percentage change, defined as: [(prevalence 2001 minus prevalence 2004) divided by prevalence 2001 multiplied by 100], was calculated and stratified per HRT category.

For calculating the duration of use, we selected in 2001 as well as in 2004 all HRT-users with at least 3-year medication history in the database before the first prescription in 2001 or 2004. Of these HRT-users we calculated the differences in proportion (2004 compared to 2001) in relation to duration of use, being: less

than 1 year, between 1 and 3 years, and more than 3-year use.

For comparing prevalences of HRT use in 2004 with 2001 we used Pearson Chi-square.

3. Results

In 2001, of the 91,873 women aged 40–74, 5182 (5.64%) received at least a HRT preparation, licenced for symptomatic treatment of vasomotor symptoms or the prevention of osteoporosis and 1618 (1.67%) received at least a vaginal low oestrogen product for vaginal atrophy. In 2004, these prevalences were 2.39 and 1.65, respectively. The prevalence in the different age categories of these two groups is shown in Fig. 1. A dramatic decrease in the prescribing of HRT is seen in all age categories, being the highest among the 50–54 (64.4% decrease) and the lowest among women aged 65–69 (40.3% decrease). For the low potency estrogens the prevalence of use did not change between 2001 and 2004. These products, aimed for vaginal atrophy, are prescribed to older women as can been seen in the figure.

Table 1 presents the percentage change in HRT use for overall HRT (all categories, excluding vaginal products), and per HRT category; combined estrogens and progestagens, estrogens only, tibolon and vaginal preparations. Between 2004 and 2001, the overall HRT prescribing decreased with 57.6%, whereas the % change for the low-potency estrogens is much lower (−6.3%) and not significantly different ($p = 0.055$). Among the HRT-users the prescribing of opposed

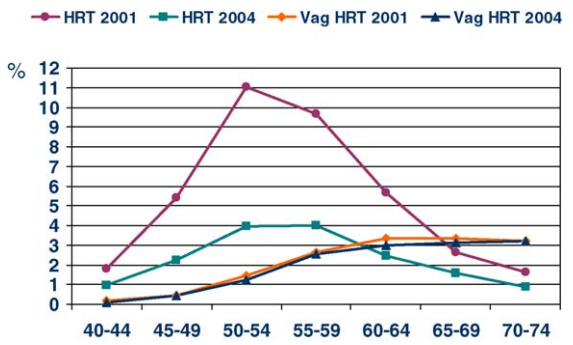

Fig. 1. Prevalences of HRT prescribing per age category in 2001 and 2004 for general HRT (combined, estrogen only and tibolon, excluding vaginal HRT) and for vaginal HRT prescribing.

HRT decreased most (66.0%), while the prevalence of tibolon changed from 0.71 in 2001 to 0.45 in 2004 (36.6% decrease).

Table 2 shows the differences in proportion (2004 compared with 2001) among HRT-users in relation to duration of use. Although the absolute numbers of HRT-users dropped from 4194 in 2001 to 2130 in 2004, the proportion of long-term users (>3 year) increased with 12.7% in 2004 compared with 2001. The changes in proportions of women who used HRT less than 1 year, and those who used it between 1 and 3 year were lower, −8 and −4.7%, respectively.

4. Discussion

Between 2001 and 2004, the prevalence of HRT use declined from 5.64 to 2.39% among women aged 40–74, whereas the use of vaginal products containing low potency estrogens did not change at all (1.76 and 1.65%, respectively). The decline in use was most pronounced among women who were prescribed combined estrogens and progestagens (65% decrease) and estrogens only (54.2% decrease). The proportion of long-term users among HRT-users increased with 12.7% in 2004 compared with 2001.

Before the release of the publications of WHI and MWS the prescribing of HRT (including vaginal applications) in The Netherlands among women aged 45–69 was 9.2% [15] and this is much lower than prevalences reported in the UK and USA. Data from the UK show a prevalence of 27.7% in 1998 among women aged 45–64 [16] and in the US these percentages vary between 38 and 50% [17,18]. In contrast with the US and the UK, HRT treatment for the prevention of cardiovascular disease and osteoporosis with consequent long-term treatment duration was never prevalent in The Netherlands. Dutch prescribers have always been very conservative in prescribing HRT, resulting in 2004 in a very low prevalence of use: 2.39 among 40–74 year olds and 2.95 in women aged 45–69.

A decline in HRT use is also evaluated with prescription claims data in the US [18,19]. Hersh et al. showed a 37% decrease of HRT prescriptions in 2003 compared with 1999 but in another study in a lower educated population (Medicaid program) the decline was less pronounced [19]. In a survey among HRT-users in New Zealand 40% stopped the use of HRT [20]. Our results

Table 1
Prevalences of HRT in women aged 40–74 per HRT category and the % change in 2004 compared with 2001

	Prevalence among women aged 40–74 years			
	2001 ($n = 91873$), *N* (prevalence)	2004 ($n = 98401$), *N* (prevalence)	Change (%)[b]	*p*-Value[a]
All HRT (excluding vaginal)	5182 (5.64)	2351 (2.39)	−57.62	<0.001
• Opposed HRT	2559 (2.79)	939 (0.95)	−65.95	<0.001
• Oestrogens only	2069 (2.25)	1018 (1.03)	−54.22	<0.001
• Tibolon	652 (0.71)	440 (0.45)	−36.62	<0.001
Low-potency estrogens	1618 (1.76)	1621 (1.65)	−6.25	0.055

[a] *p*-Value indicates whether prevalences differ between 2001 and 2004 using Pearson Chi-square.
[b] % Change: $\frac{\text{prevalence 2001} - \text{prevalence 2004}}{\text{prevalence 2004}}$.

Table 2
Number of HRT-users in women aged 40–74 according to the duration of use (<1, 1–3 and >3 year) in 2001 and 2004, and the difference in proportion in 2004 compared with 2001

Duration of use	Number of HRT (excluding vaginal HRT) users (40–74 year) (at least 3 years data available)		
	2001 *N* (%)	2004 *N* (%)	Difference in proportion 2004 vs. 2001 (%)
<1 year	1179 (28.1)	429 (20.1)	−8.0
Between 1 and 3 years	850 (20.3)	332 (15.6)	−4.7
>3 years	2165 (51.6)	1369 (64.3)	+12.7
Overall	4194 (100)	2130 (100)	

show a decline of 57.6% among women aged 40–74 who received HRT (excluding vaginal preparations). The different percentage decline seen in the studies can be explained by the method used, the age groups involved and the definition of the HRT. As is shown in this study, the decline among the different age categories varied from 64% (50–54 years) to 40% (65–69 years). Studies among different age groups will reveil different percentages change. We also illustrated that the use of vaginal estrogen products, used for vaginal atrophy, did change only marginally (−6%), whereas the decline of opposed HRT in the same age category (40–74 years) declined drastically (66%). Combining both types of HRT will consequently result in lower percentages change.

Although the Dutch recommendations stated that HRT should be used only in women with severe complaints and during of short time, we see in 2004 among HRT-users a greater proportion of long-term users (>3 year) 64.3% compared with 51.6% in 2001, whereas the proportion of short-term users (<1 year and between 1–3 years) declined. One explanation may relate to the beneficial effects in women with severe menopausal complaints. A recent Dutch survey showed that short-term considerations prevail in deciding to continue or stop the use of HRT for women who used the medication for a longer time [21].

In summary, we described a 57.6% decrease in the prevalence of HRT-users in 2004 compared with 2001. This 57.6% decrease in a population with an existing low prevalence of HRT use resulted in 2004 in an overall prevalence of less than 3%. The prevalence of vaginal low-potency estrogens did not change in the same population. We will monitor future patterns of HRT use to know whether this decrease will be sustained.

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